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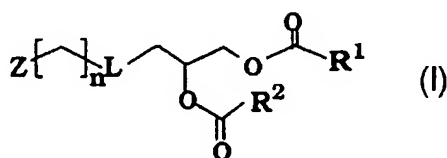
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60/158,693 8 October 1999 (08.10.1999) US
- (71) Applicant: ALZA CORPORATION [US/US]; 1900 Charleston Road, P.O. Box 7210, Mountain View, CA 94039-7210 (US).
- (72) Inventors: HUANG, Shi, Kun; 18798 Madison Avenue, Castro Valley, CA 94546 (US). ZALIPSKY, Samuel; 1202 Truman Street, Redwood City, CA 94061 (US). ZHANG, Wei-Ming; 1550 5th Avenue, Apt. #202, San Francisco, CA 94122 (US). JIN, Bei; 4546 Cape View Drive, Union City, CA 94587 (US). QUINN, Yolanda, P.; 631 Larchmont Drive, Daly City, CA 94015-3060 (US).
- (54) Title: NEUTRAL-CATIONIC LIPID FOR NUCLEIC ACID AND DRUG DELIVERY
- (57) Abstract: A lipid represented by formula (I), wherein each of R<sup>1</sup> and R<sup>2</sup> is an alkyl or alkenyl chain having between about 8 to about 24 carbon atoms; n = 1-20; L is selected from the group consisting of (i) -X-(C=O)-Y-CH<sub>2</sub>-, (ii) -X-(C=O)-, and (iii) -X-CH<sub>2</sub>-, wherein X and Y are independently selected from oxygen, NH and a direct bond; and Z is a weakly basic moiety that has a pK of less than about 7.4 and greater than about 4.0 is described.
- (74) Agents: SIMBOLI, Paul, B. et al.; Alza Corporation, 1900 Charleston Road, P.O. Box 7210, Mountain View, CA 94039-7210 (US).
- (81) Designated States (*national*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW.
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- Published:  
— with international search report
- (88) Date of publication of the international search report:  
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- For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.



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# INTERNATIONAL SEARCH REPORT

International Application No  
PCT/US 00/27974

A. CLASSIFICATION OF SUBJECT MATTER  
IPC 7 C07D233/54 A61K47/00 A61P43/00 C07H5/06 C07C271/28

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)  
IPC 7 C07D A61K A61P C07H C07C

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

CHEM ABS Data

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 97 00241 A (BOEHRINGER MANNHEIM GMBH) 3 January 1997 (1997-01-03) claims	1, 19
A	US 5 891 468 A (FRANCIS J. MARTIN ET AL.) 6 April 1999 (1999-04-06) column 1 -column 5	1, 19
P, X	US 5 965 434 A (JON A. WOLFF ET AL.) 12 October 1999 (1999-10-12)  * complete document *	1, 5, 8, 10, 11, 19, 23
P, X	WO 00 30444 A (VANDERBILT UNIVERSITY) 2 June 2000 (2000-06-02) * complete document *	1, 19

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☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

### \* Special categories of cited documents:

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
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- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

- \*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- \*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- \*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- \*G\* document member of the same patent family

Date of the actual completion of the international search

30 July 2001

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Name and mailing address of the ISA  
European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040. Tx. 31 651 epo nl.  
Fax: (+31-70) 340-3016

Authorized officer

Van Bijlen, H

## INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 00/27974

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
E	WO 01 26625 A (ALZA CORPORATION) 19 April 2001 (2001-04-19) claims -----	1-33

## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 1-33 ( all partially )

Present claims 1, 19 and 30 ( and their dependent claims ) relate to a composition, respectively a general formula and a method for delivering and they all relate to a formula containing a substituent Z which is not defined in structural terms but is defined as " a weakly basic moiety that has a pK of less than about 7.4 and greater than about 4.0 ". The use of such a parameter in the present context is considered to lead to a lack of clarity within the meaning of Article 6 PCT. It is impossible to compare the parameter the applicant has chosen to employ with what is set out in the prior art. The lack of clarity is such as to render a meaningful complete search impossible. Consequently the search and the search report can only be considered complete for compounds of the general formula of claim 19 wherein Z is a substituent as in the figures 3A-3C of the present application.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 00/27974

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9700241 A	03-01-1997	DE 19521412 A AT 199246 T AU 713587 B AU 6355396 A CA 2224566 A CN 1193316 A DE 59606469 D EP 0835238 A HU 9802738 A JP 11507659 T NO 975853 A US 6060455 A	19-12-1996 15-03-2001 02-12-1999 15-01-1997 03-01-1997 16-09-1998 29-03-2001 15-04-1998 29-03-1999 06-07-1999 16-02-1998 09-05-2000
US 5891468 A	06-04-1999	US 6056973 A US 6224903 B AU 715063 B AU 4987897 A BR 9712230 A EP 0932391 A WO 9816202 A	02-05-2000 01-05-2001 13-01-2000 11-05-1998 25-01-2000 04-08-1999 23-04-1998
US 5965434 A	12-10-1999	NONE	
WO 0030444 A	02-06-2000	AU 1830200 A	13-06-2000
WO 0126625 A	19-04-2001	WO 0126629 A	19-04-2001

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